Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-11 (cancelled)

12. (Currently amended) A method for generating a secondary library of ~~scaffold~~ protein variants of a target protein comprising:

a) ~~receiving a library of primary sequences generated utilizing a force field calculation~~ inputting the coordinates of said target protein into a computer;

b) ~~generating a probability distribution table of amino acid residues in a plurality of variant positions from said primary sequences; and~~ utilizing a forcefield calculation to generate a primary library comprising a plurality of primary variant amino acid residues at primary variant positions;

c) ~~combining a plurality of said amino acid residues to generate a secondary library of secondary sequences; wherein at least one of said secondary variants is different from said primary variants.~~ computationally generating a probability distribution table of variant amino acid residues in a plurality of said primary variant positions; and

d) combining a plurality of said primary variant amino acid residues to generate a secondary library of secondary variant proteins.

13. (Previously presented) A method according to claim 12, wherein said force field calculation is Self-Consistent Mean Field (SCMF).

Claims 14-20 (Cancelled)

21. (Currently amended) A method according to claim[[s]] 12 ~~or 16 further comprising synthesizing a plurality of said secondary sequences~~ wherein said combining comprises:

a) generating a set of oligonucleotide probes each encoding at least one of said primary variant amino acid residues;

b) using said probes in a polymerase chain reaction (PCR) to generate a plurality of oligonucleotide sequences, each encoding said secondary variant sequences; and

c) producing said secondary variant sequences in host cells transformed with said oligonucleotide sequences.

22. (Currently amended) A method according to claim 21 wherein said ~~synthesizing~~ PCR is ~~done by~~ multiple PCR wherein said probes are pooled.

23. (Currently amended) A method according to 22 wherein said ~~pooled oligonucleotides~~ probes are added in equimolar amounts.

24. (Currently amended) A method according to claim 23 wherein said ~~pooled oligonucleotides~~ probes are ~~added~~ combined in amounts that correspond to the frequency of the ~~mutation~~ said variant amino acid residues in said probability distribution table.

Claim 25 (cancelled)

26. (new) A method for generating a secondary library of protein variants of a target protein comprising:

(A) generating a primary library comprising:

(i) inputting the coordinates of a target protein with variable residue positions;
(ii) establishing a group of potential rotamers for each of said variable residue positions, wherein the group of potential rotamers for at least one of said variable residue position has a rotamer selected from each of at least two different amino acid side chains; and
(iii) analyzing the interaction of each of said rotamers with plurality of said rotamers at a plurality of variable residue positions and all or part of the remainder of said protein to generate a primary library of primary sequences;
(B) generating a probability distribution table of amino acid residues from said primary library in a plurality of variant positions from said primary sequences; and
(C) combining a plurality of said amino acid residues to generate a secondary library of secondary sequences comprising secondary variants; wherein at least one of said secondary variants is different from said primary variants;
wherein at least one of said analyzing, generating or combining steps comprises using a force field calculation.

27. (new) A method according to claim 26 wherein said analyzing step utilizes a force field calculation.

28. (new) A method according to claim 27 wherein said generating step utilizes a force field calculation.

29. (new) A method according to claim 28, wherein said force field calculation is Self-Consistent Mean Field (SCMF).

30. (new) A method for generating a secondary library of protein variants of a target protein comprising:
(A) generating a primary library comprising:
(i) inputting the coordinates of a target protein with variable residue positions;
(ii) establishing a group of potential rotamers for each of said variable residue positions, wherein the group of potential rotamers for at least one of said variable residue position has a rotamer selected from each of at least two different amino acid side chains; and
(iii) analyzing the interaction of each of said rotamers with plurality of said rotamers at a plurality of variable residue positions and all or part of the remainder of said protein to generate a primary library of primary sequences optimized for at least one scoring function;
(B) generating a probability distribution table of amino acid residues from said primary library in a plurality of variant positions from said primary sequences; and
(C) combining a plurality of said amino acid residues to generate a secondary library of secondary sequences comprising secondary variants; wherein at least one of said secondary variants is different from said primary variants.

31. (new) A method according to claim 30, wherein said scoring function is selected from the group consisting of a van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

32. (new) A method for generating a secondary library of protein variants of a target protein comprising:

(A) generating a primary library comprising:

(i) inputting the coordinates of a target protein with variable residue positions;

(ii) establishing a group of potential rotamers for each of said variable residue positions, wherein the group of potential rotamers for at least one of said variable residue position has a rotamer selected from each of at least two different amino acid side chains;

(iii) analyzing the interaction of each of said rotamers with plurality of said rotamers at a plurality of variable residue positions and all or part of the remainder of said protein; and

(iv) utilizing a force field calculation to generate a primary library of primary sequences;

(B) generating a probability distribution table of amino acid residues from said primary library in a plurality of variant positions from said primary sequences; and

(C) combining a plurality of said amino acid residues to generate a secondary library of secondary sequences comprising secondary variants; wherein at least one of said secondary variants is different from said primary variants.